"DESIGN AND DEVELOPMENT OF MICROSPONGE GEL FOR TOPICAL DELIVERY OF ANTIFUNGAL DRUGS"

SYNOPSIS

SUBMITTED FOR REGISTRATION OF

THE DEGREE OF

DOCTOR OF PHILOSOPHY

IN THE SUBJECT

PHARMACEUTICAL SCIENCES

At

SARDAR PATEL UNIVERSITY, BALAGHAT (M.P.)

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2019-20

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1. INTRODUCTION

1. Introduction

Topical drug delivery systems are formulated to enter in to the systemic circulation, where skin serves as the portal of entry to the drug and various formulations made available in the market are creams, lotions, ointments, TDS etc. (Prasad MSC, 2011).

Main drawbacks of former topical preparations are the drug doesn't reaches the systemic circulation in sufficient amounts and they are topically localized and no such vehicles and ingredients are incorporated for the controlled release of active medicament. The effective therapy of the disease often seen high concentration of active medicament and produces the skin irritation problems reported in some research studies and also uncontrolled evaporation of active agents, potential incompatibility of drug with vehicles. (Prasad MSC, 2011).

Thus the microsponge should remain maximum time at the skin and below the epidermis and release the medicament slowly. For these reasons microsponge should meet the following characteristics (Prasad MSC, 2011):

- ·Microsponges should be uniform, spherical having the cross linked polymeric system, non collapsible structure consisting of porous void space for the large entrapment of various active ingredients in the spaces and it offers higher shear strength which are commonly used in the area of creams, lotions, powders, having maximum payload of (50% to 60%), and inter connected void space of particle size range5-500μm.[2]
- ·It should be non irritant, non mutagenic, non toxic, non greasy.
- ·It should be Stable at high temperature, and high shear.
- ·It should shows improved stability.
- ·It should have advanced Oil control i.e. Absorbs up to 6 times its weight without drying.
- It should show extended release up to 12 hours.

Microsponge have advantages over the conventional dosage forms where the conventional dosage forms produce the localization of active medicament in the surface of the skin producing toxicity and skin irritation in BPO. This is avoided by the microsponge drug delivery by Microsponges must meet following requirements: (Prasad MSC, 2011)

- If the drug is typically non-polar material, it should create the porous structure this is called porogen.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers and polymers.
- It should be stable in contact with polymerization catalyst and conditions of polymerization.
- Release can be controlled through diffusion or other triggers such as moisture, pH, friction, or temperature.

1.1 Benefits of Microsponge Technology **(Gupta A, 2016)**

- Microsponge technology offers:
- Enhanced product performance.
- Extended release.
- Reduced irritation and hence improved patient compliance.
- Improved product elegancy.
- Improved oil control as it can absorb oil up to 6 times its weight without drying.
- Improved formulation flexibility.
- Improved thermal, physical, and chemical stability.

1.2 Characteristics of the Materials **(Gupta A, 2016)**

- Entrapped In Microsponges.
- Most liquid or soluble ingredients can be entrapped in the particles. Actives that can be entrapped in microsponges must meet following requirements.
- It should be either fully miscible in monomer or capable of being made miscible by addition of small amount of a water immiscible solvent.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers.

- It should be stable in contact with polymerization catalyst and conditions of polymerization.

1.3 Potential Advantages of the Microsponge Drug Delivery System **(Gupta A, 2016)**

- Microcapsules cannot usually control the release rate of the active pharmaceutical ingredients (API). Once the wall is ruptured the API contained within the microcapsules will be released. Can the MDS can do it, is the question.
- Liposomes suffer from a lower pay load, difficult formulation, limited chemical stability, and microbial instability. Do the MDS have a wide range of chemical stability and are they easy to formulate
- MDS have stability over a pH range of 1 – 11.
- Microsponges have stability up to temperature 130°C.
- Microsponge having Pay load is up to 50 – 60%.
- They have free flowing and cost effective.
- Microsponges are microscopic spheres capable of absorbing skin secretions, therefore, reducing oiliness and shine from the skin.

1.4 Properties of the Actives for the Entrapment into Microsponges **(Gupta A, 2016)**

- It should be either fully miscible in a monomer or capable of being made miscible by the addition of a small amount of a water-immiscible solvent.
- It should be water immiscible or at most only slightly soluble.
- It should be inert to monomers and should not increase the viscosity of the mixture during formulation.
- It should be stable when in contact with the polymerization catalyst and under conditions of polymerization.
- The spherical structure of the microsponges should not collapse**.**

2. LITERATURE REVIEW

2.1 Sharma P *et al* (2019) was studied the Eudragit RL 100 facilitated microsponges by the double emulsification technique (Quasi emulsion technique) and subsequently dispersed in a carbopol gel base for controlled delivery of roxithromycin to the skin. The microsponges formulations were prepared by quasiemulsion solvent diffusion method employing Eudragit RL 100 as a polymer.

2.2 Dombe S *et al* (2017) was studied novel drug delivery system containing oxiconazole nitrate microsponges and to prepare microsponge gel. The microsponges was prepared by quasi-emulsion solvent diffusion method by using polymer eudragit S-100 and eudragit L-100. All the formulated microsponges was subjected for various evaluation parameters such as production yield, encapsulation efficiency, particle size analysis and *in vitro* drug release study. The optimised microsponge formulation F3 and F9 were further formulated as gel formulation for topical delivery. Prepared gel was evaluated for physical Parameter.

2.3 Moin A *et al* (2016) was studied the Microsponges were prepared using quasi‐emulsion solvent diffusion method using Eudragit S‐100. In the direction of optimization, the effect of formulation variables (drug‐polymer ratio and amount of emulsifier) and diverse factors affecting physical characteristics of microsponge were investigated as well. Fabricated microsponges were characterized by differential scanning calorimetry, Fourier transform‐infrared, scanning electron microscopy (SEM), particle size analysis, and also evaluated for drug content, encapsulation efficiency, *in vitro* drug release and *in vitro* antifungal activity.

2.4 Kadnor A *et al* (2015) was studied the Microsponges loaded with sertaconazole nitrate were prepared by using quasi emulsion solvent diffusion with five different proportions of the polymer (Eudragit RS 100). The developed microsponges were analyzed for particle size,production yield, entrapment efficiency and drug content. Scanning electron microscopic images of microsponges revealed that they are spherical in shape and contain pores.

2.5 Hussain H *et al* (2015) was studied the ethyl cellulose facilitated microsponges were prepared by the double emulsification technique (Quasi emulsion technique) and subsequently dispersed in a carbopol gel base for controlled delivery of diclofenac sodium to the skin. The microsponges formulations were prepared by quasiemulsion solvent diffusion method employing ethyl cellulose as a polymer. The compatibility of the drug with formulation components was established by Fourier Transform Infra-Red (FTIR) spectroscopy.

2.6 Kumar JR *et al* (2013) was studied the Microsponge containing ketotifen drug with three different proportions of ethyl cellulose and drug were obtained successfully using quasi-emulsion solvent diffusion method. These formulations were studied for particle size and physical characterization. These microsponges enriched gel formulation were prepared by using 2 and 3 % w/w of SCMC and studied for viscosity, pH, gel strength, spreadability, bioadhesive force, drug content, in vitro release, HPLC and SEM analysis. The viscosity of microsponges enriched gel was found to be in the range 1299 to 1600 centipoises. The maximum gel strength and mucoadhesive force was found to be up to (8.12 sec) and (32.32 dynes/cm2) respectively. The formulations exhibited spreadability (22.88 gm.cm/sec), The optimized formulations were able to release the drug up to 8 hours.

3. AIM AND OBJECTIVE

3.1 Aim

To Design and develop microsponge gel for topical delivery of antifungal drugs.

3.2 Objective

1. To provide prolonged and constant therapeutic effect.
2. To reduce the dosing frequency and therefore improve the patient compliance
3. To Decrease in toxicity while maintaining therapeutic effects.
4. To provide controlled, sustained and targeted delivery of the drug.
5. Development of safe medicine.

4. PLAN OF WORK

4.1. Literature survey

4.2. Procurement of Drugs and Excipients

4.3. Preformulation study

- Physical Characteristics
- Melting Point
- Solubility studies

4.4. Formulation of Microsponges by quasi-emulsion solvent diffusion method.

4.6. Evaluation of Microsponges

a) Percent Yield

b) Drug-Content

c) Particle Size

d) Spreadability Test

e) pH Determination

f) Viscosity measurement

g) *In vitro diffusion studies using KC cell*

4.7 Results and Discussion

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